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Research Article

Effect of beta blockers on central aortic pressure in African-Americans

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Abstract

The objective of this study was to evaluate the vascular effects of heart rate (HR) reduction with BB therapy in African Americans (AA). Beta-blockers (BB) offer less cardiovascular protection than other hypertensive drugs. Studies of Caucasian subjects suggest this may be due to an adverse effect of HR lowering on arterial wave reflection. We studied 506 subjects (age 63 ± 14 years, 52% were treated with BB). Central systolic (C-SBP) and pulse pressure (C-PP), augmented pressure (AP), and augmentation index (AI) were obtained via applanation tonometry (Sphygmocor). On univariate analysis, HR correlated inversely with BB use, C-SBP, AP, and AI (all $P < .001$), but not P-SBP. Multivariate analysis showed P-SBP and HR to be major determinants of C-SBP ($R^2 = 0.95$). Generalized linear model analysis showed higher C-SBP ($P < .05$) and C-PP ($P = .04$), but similar P-SBP ($P = .24$) in the BB group. After HR adjustment, differences in C-SBP, C-PP, AI, and AP were attenuated, suggesting HR to be a determinant of C-SBP. BB use is associated with higher C-SBP and lower PPA in hypertensive AA despite similar P-SBP. C-SBP is HR-dependent. HR reduction with BB accounts for less effective central blood pressure control in AA, similar to that reported in Caucasians. J Am Soc Hypertens 2011;5(2):94–101. Published by Elsevier Inc on behalf of American Society of Hypertension.

Keywords: Beta blocker; hypertension; African Americans; arterial wave reflection.

Introduction

Beta-blockers (BBs) have long been recommended as first-line treatment for hypertension. In recent years, their benefits with regard to cardiovascular risk reduction have come into question. Large meta-analyses have found BBs inferior to other medications in reducing stroke and mortality.[1–4] Several explanations have been proposed for these findings. BBs are known to portend deleterious effects on glucose and lipid metabolism.[5,6] Specifically, these agents worsen insulin resistance and increase triglycerides in a dose-dependent manner. In addition, these agents do not directly block the renin-angiotensin-aldosterone pathway.[7] More recently, BBs have been found less effective in reducing central aortic BP despite brachial artery blood pressure (BP) lowering that is similar to other drug classes.[8–11] The Preterax in regression of arterial stiffness in a controlled double-blind study (REASON) trial found perindopril/indapamide to lower central aortic pressure more than atenolol.[10] A recent analysis from the Conduit Artery Function Evaluation analysis (CAFÉ) of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) study suggested that heart rate (HR) lowering associated with atenolol resulted in higher central aortic BP.[12,13] Higher central aortic BP was proposed to be caused by greater wave reflection at lower HRs. Prior studies have suggested BB to adversely affect wave reflection.[14] In the CAFÉ analysis, HR was inversely correlated with central aortic systolic and pulse pressures, a finding limited to subjects enrolled into the CAFÉ substudy of the ASCOT trial.[13] Among the 1900 hypertensive subjects, 86% were Caucasian, leaving a total of 295 subjects of other ethnicities.

Hypertension is more prevalent and severe in African Americans (AA) and more frequently causes target organ injury in this population.[15] Whether HR reduction with BBs is a major mechanism accounting for less effective central aortic pressure reduction in AA remains unknown. The importance of this question is underscored by the fact that when given as monotherapy, BB are relatively less effective than diuretics and calcium channel blockers

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in lowering peripheral BP in AA.[16] It remains unclear as to whether the difference in brachial artery and central aortic pressure is HR dependent and related to BB therapy in AA.

Methods

We prospectively studied 506 HTN AA subjects (age 63 ± 14 years, 36% male) with a history of hypertension. Patients with a history of heart failure were excluded. Fifty-two percent were treated with BB. Brachial arterial (P), systolic (SBP), diastolic (DBP), and mean arterial pressure were obtained via an automated BP device (Omron HEM-780, Omron Healthcare, Matsuzaka City, Mie, Japan). Pulse pressure (PP) is defined as the difference between systolic and diastolic BPs. Central systolic pressure (C-SBP), pulse pressure (C-PP), central augmented pressure (AP), augmentation index (AI) and pulse pressure amplification (PPA; PPP/CPP) were derived from the radial artery waveform obtained by applanation tonometry (Sphygmocor, Atcor Medical, Sydney, Australia) and use of a validated transfer function.[17] AP was defined as the proportional increase in systolic pressure from the reflected wave. AI was defined as the AP expressed as a percentage of the PP.[18] The incident (P1) or forward pressure wave amplitude is defined as the initial upstroke of the reflected pressure wave minus the minimum diastolic pressure.[18] Round trip travel time (Tr) is the time of the pressure wave to and from the major reflecting sites in the body, and is measured as the time from the initial upstroke of the pressure wave to P1. The systolic duration of the reflected pressure wave (ΔTr) was determined from the inflection point to the incisura. Sequential recordings of arterial pressure waveform at the carotid and radial arteries were used to measure carotid-radial pulse wave velocity (PWV) using the Sphygmocor device. Distances from the suprasternal notch to the carotid sampling site (distance A) and from the suprasternal notch to the radial artery (distance B) were measured. Pulse wave velocity distance was calculated as distance B minus distance A. PWV was calculated as the ratio of the distance in meters to the transit time in seconds. Clinical data, including medical history, smoking status, and medications, were obtained from patient interview and chart review. Inclusion criteria were age ≥18 years, adequate radial and carotid pulses to obtain the applanation tonometry study, and sinus rhythm. Risk factors evaluated in this study included age, body mass index, hyperlipidemia, diabetes mellitus, congestive heart failure, hypertension, chronic renal insufficiency, known coronary artery disease defined by patient history or an abnormal stress imaging study, previous stroke, and smoking status (current cigarette use). These cardiovascular risk factors were defined either as self-reported, documented diagnosis obtained from chart review, or current treatment with medication. Informed consent was obtained from all participants and the University Hospital of Brooklyn's institutional review board approved the study.

Data were expressed as mean ± standard deviation. Continuous variables were compared using Student's paired *t*-test and the chi-square test was used to compare frequencies of dichotomous variables. Continuous variables were assessed using Spearman's correlation. Differences in BPs between BB and non-BB groups were assessed before and after HR adjustment using analysis of variance (ANOVA). Stepwise multivariate linear regression was used to assess the independent predictors and their relative contribution to the central pressures. All statistical analyses were achieved using SPSS 17.0 software (SPSS Inc, Chicago, IL). A P value $< .05$ was considered to be statistically significant.

Results

The BB and non-BB groups were similar in terms of age, height, weight, and BMI (Table 1). Metoprolol was the most frequently used BB. On univariate analysis, HR was inversely correlated with C-SBP ($r = -0.14$, $P = .001$), but not with P-SBP ($r = -0.03$, $P = .55$). Figure 1 represents the relation of deciles of HR with P-SBP and C-SBP. The beta of −2.3 noted in Figure 1 indicates a CSBP decrease of 2.3 mm Hg for each 10-beat increase in HR. Similarly, HR more strongly inversely correlated with C-PP ($r = -0.31$, $P < .001$) than with P-PP ($r = -0.095$, $P = .03$). HR directly correlated with PPA ($r = 0.61$, $P < .001$) indicating greater pulse pressure differences with higher heart rates. On multivariate analyses (corrected for height, weight, gender, age, BB use, angiotensin-converting enzyme inhibitor, calcium channel blocker, thiazide, or loop diuretic use), P-SBP and HR accounted for 95% of the variability in C-SP. Similarly, P-PP and HR accounted for 92.4% of C-PP variability. No other antihypertensive medications other than BB medications were associated with higher C-SBP ($B = 0.88$, $P = .004$) and CPP ($B = 0.79$, $P = .007$).

ANOVA showed no significant difference in P-SBP between BB and non-BB groups (141.34 ± 25 vs. 138.85 ± 22, $P = .24$). The BB group had higher C-SBP (130.36 ± 24 vs. 126.39 ± 20, $P < .05$), and C-PP (47.71 ± 19 vs. 44.37 ± 16, $P = .04$). After full HR adjustment, the differences in C-SBP, C-PP, AP, AI, PPA, and peripheral minus central SBP and PP were attenuated, suggesting the difference between central and peripheral pressures is in part from HR (Table 2). On univariate analysis of individual BBs, HR correlated to PPA, peripheral-central SBP, and peripheral-central PP for metoprolol ($r = 0.59$, $P < .001$; $r = 0.40$, $P < .001$; $r = 0.45$, $P < .001$, respectively), atenolol ($r = 0.63$, $P < .002$; $r = 0.43$, $P < .035$; $r = 0.58$, $P < .004$, respectively), and labetalol/carvedilol combination ($r = 0.39$, $P < .02$; $r = 0.38$, $P < .02$; $r = 0.47$, $P < .005$, respectively).

Univariate analysis demonstrated both PPA and HR to be inversely correlated with ΔTr, P1, AP, AI, and Tr. Figure 2 represents the relation of HR with the different indices of